Attached hereto is a marked up version of the changes made to the claims by the current Amendment and Response. The attached page is captioned **"Version with markings to show changes made."**

Drawings

Applicants have submitted final, corrected drawings.

Rejection Under 35 USC §112, First and Second Paragraphs

Applicants deleted the "immunogenic derivative" language from the claims to address the Examiner's Section 112 rejections. The claims have been amended to include the language "mutant". Support for this language can be found at page 3, lines 6-9 of the specification where it states that: "Derivatives encompassed within the present invention also include mutated proteins. The term "mutated" is used herein to mean a molecule which has undergone deletion, addition or substitution of one or more amino acids using well known techniques for site directed mutagenesis or any other conventional method."

Applicants respectfully submit that the amended claims comply with the requirements of Section 112, and the rejections should be withdrawn.

Rejection Under 35 USC §103(a)

The examiner rejected claims 32, 33, 34, 36, 40-49 and 54 under 35 USC §103(a) as obvious over Schluesener and Hinkula, claim 35 further in view of Gaynor, claims 50-53 further in view of Berman et al. and claims 37-39 further in view of Forsgren.

Schluesener discloses the use of a Tat peptide fragment in the delivery of non-HIV epitopes. The teaching of this reference differs from the present invention in a number of ways. Initially, it is important to note that the general teaching of this document is in the area of protection against autoimmune diseases. Further, the Tat peptide is not being used to provide protection against HIV in any way, merely to deliver epitopes to provide protection against autoimmune diseases. There is no teaching to suggest fusing Tat to an HIV peptide or epitope. There is certainly no suggestion of fusing to Nef, as acknowledged by the examiner. There is no suggestion to use the construct to provide protection against HIV. Furthermore,

one skilled in the art is not taught that Tat can be fused with an HIV antigen, that Tat can be used with a full length protein, or that a Tat fusion would provide a protective vaccine.

The second reference cited by the examiner, Hinkula, also differs substantially from the present invention. Hinkula is only concerned with DNA delivery, and not protein delivery. There is no teaching of fusion proteins. There is no specific teaching that the combination of Nef and Tat would be effective. The Examiner cites page Hinkula 5538, last paragraph as an indication that one skilled in the art would construct a vaccine with multiple proteins or glycoproteins. This statement does not explicitly teach the use of multiple different proteins. Indeed, Hinkula teaches that multiple proteins may be necessary due to the polymorphism of the human population. Thus the teaching of Hinkula applies equally to a vaccine containing multiple different versions of the same protein, which allows a vaccine to accommodate polymorphism. There is no explicit teaching that more than one protein is required.

Contrary to the Examiner's assertion on page 7 of the official action, Schluesener does not teach the formulation of a polyvalent immunogen using multivalent linked HIV antigens. Only one HIV component is taught. Furthermore, Hinkula does not unambiguously teach multiple HIV antigens, merely that a vaccine must address the issue of polymorphism in the human population. This can be addressed by multiple versions of the same protein.

Accordingly, one skilled in the art would not consider combining the two principal references especially since one is in the field of protection against experimental nervous system auto immune diseases, and the other is in the field of HIV. Even if these references are combined, the skilled person cannot arrive at the present invention. It is clear that one teaches a DNA approach, and the other a peptide approach. Neither teaches a combination of two full-length proteins in a fusion state. Most important, Schluesener does not require the TAT to be an immunogenic component only a delivery vehicle. Schluesener only teaches the use of a TAT fragment as a carrier. There is no indication that the TAT protein has any immunogenic epitopes or would provide any protective response.

Gaynor, Berman et al. and Forsgren add nothing that would allow one skilled in the art to combine the two principal references to arrive to the present invention, or to take the principal references separately and combine them with the teachings of Gaynor, Berman et al. and Forsgren to arrive to the present invention.

Withdrawal of the rejection of the claims under 35 U.S.C. §102(a), is respectfully requested

Applicants respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claims 32-36 and 54 have been amended as follows:

32. (Twice Amended) An immunogenic composition which comprises a protein comprising

(a) an HIV Tat protein or [~~an immunogenic derivative~~] a mutant thereof linked to an HIV Nef protein or [~~an immunogenic derivative thereof~~] a mutant thereof; or

(b) an HIV Nef protein or [an immunogenic derivative] a mutant thereof linked to an HIV Tat protein or [~~an immunogenic derivative thereof~~] a mutant thereof; or

(c) an HIV Nef protein or [an immunogenic derivative] a mutant thereof linked to an HIV Tat protein or [~~an immunogenic derivative thereof~~] a mutant thereof and a fusion partner,

in admixture with a pharmaceutically acceptable excipient.

33. (Twice Amended) A composition as claimed in claim 32, comprising a Tat-Nef fusion protein or [~~an immunogenic derivative thereof~~] a mutant thereof.

34. (Twice Amended) A composition as claimed in claim 32, comprising a Nef-Tat fusion protein or [~~an immunogenic derivative thereof~~] a mutant thereof.

35. (Twice Amended) A composition according to claim 32, wherein the [~~derivative of the~~] Tat protein is [~~an immunogenic~~] a mutated Tat protein.

36. (Twice Amended) A composition according to claim 32, wherein the [~~derivative of the~~] Nef protein is [~~an immunogenic~~] a mutated Nef protein.

54. (Twice Amended) A protein comprising an HIV Tat protein or [~~an immunogenic derivative thereof~~] a mutant thereof linked to an HIV Nef protein or [~~an immunogenic derivative thereof~~] a mutant thereof in Nef-Tat or Tat-Nef orientation.